

Commentary

Debate: Unstable angina – when should we intervene?

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Abstract

The prognosis of patients who present with non-ST segment elevation acute coronary syndromes (ACS) is guarded. These patients can be risk-stratified on the basis of symptom complex, electrocardiographic ST segment depression, obvious hemodynamic compromise and particularly on the basis of serum troponin level. An elevated troponin level determines risk and also predicts the degree of benefit from treatment with either low molecular weight heparin or platelet glycoprotein (GP) IIb/IIIa blockade. Higher risk patients should undergo early coronary angiography and myocardial revascularization as indicated and feasible. Although studies performed before the advent of coronary stenting and adjunctive platelet GP IIb/IIIa blockade suggested increased hazard for patients undergoing early intervention, recent experience cited herein supports an in-hospital and long-term clinical benefit for the aggressive approach. Here, I propose an algorithm for risk stratification and triage of appropriate patients for adjunctive pharmacotherapy and early revascularization.

Keywords: acute coronary syndromes, unstable angina

Introduction

In the current era of coronary stenting and adjunctive platelet GP IIb/IIIa blockade, efficient and effective therapy can be offered to patients who present with non-ST segment elevation ACS. Empirically defined durations of medical 'stabilization' offer no specific advantage to this patient population (unstable angina; non-ST elevation acute myocardial infarction). Unfortunately, prior trials comparing an 'aggressive' (invasive) versus 'conservative' (non-invasive) strategy were performed before the advent of platelet GP IIb/IIIa blockade and coronary stenting [1,2]. These studies identified excess 'hazard' for early interven-

tion and appeared to confirm prior retrospective analyses which had suggested that percutaneous coronary intervention (PCI), performed at the time of diagnostic catheterization (ad hoc) [3,4] or during the first week following presentation for unstable angina [5], was associated with an increased rate of procedural failure and major hospital complications. Thus, the current Agency for Health Care Policy and Research (AHCPR) guidelines published in 1994 promote 'conservatism' to avoid 'early hazard' and, unfortunately, define treatment strategy (invasive versus conservative) before adequately assessing patient risk [6]. In light of recent developments in interventional technology

and adjunctive pharmacology as well as in our understanding of accurate risk stratification, it is most appropriate at this time to reevaluate our approach to patients with non-ST segment elevation ACS. Let us start by defining the magnitude and significance of this problem.

Non-ST segment elevation ACS has become the most frequent admission diagnosis in the United States Medicare population. In addition, the prognosis of this syndrome with 'conventional' therapy (aspirin, unfractionated heparin, nitrates, beta blockers and no revascularization strategy) remains guarded. Analysis of the control arms for randomized trials of new treatment modalities reveals an incidence of death or nonfatal myocardial infarction of 8–15% at 30 days and 10–20% at 6 months following enrollment [1,7–11]. Observations on the natural history of unstable angina confirm an alarming incidence of death or myocardial infarction (17%) and the requirement for symptom-driven revascularization by either angioplasty (30%) or coronary artery bypass graft surgery (CABG) in 27% of patients at one year following presentation [12]. The ineffectiveness of the conventional-conservative treatment strategy has been compounded by inefficiency. Average published hospital lengths of stay for the diagnosis of unstable angina range from 4–14 days internationally (5 days in the USA) [13–15]. Indeed, recent data from the European ENACT registry of unstable angina demonstrate an average intensive care unit stay of 3.4 days with a total hospital stay of 8.4 days [15]. These observations point to the need for more effective and efficient treatment strategies for patients who present with non-ST elevation ACS.

Advances in adjunctive pharmacotherapy

Randomized controlled trials have established the superiority of dalteparin (versus placebo) [16] and enoxaparin (versus unfractionated heparin) [8,17] for reducing the occurrence of death or nonfatal myocardial infarction, requirement for urgent revascularization or recurrence of angina pectoris in patients who present with non-ST elevation ACS [18]. The sequence of subcutaneous dalteparin therapy followed by random allocation to early revascularization (average 6 days) reduced the composite endpoint of death or nonfatal myocardial infarction to 6 months compared with subcutaneous dalteparin followed by a conservative (no revascularization) strategy [19]. A preliminary experience with PCI following 48 h subcutaneous enoxaparin therapy, from the ESSENCE trial performed in France, reported an extremely low rate of major cardiac events and supports an 'early invasive' strategy for this patient population [20]. Separately conducted placebo-controlled randomized trials have proven the efficacy of platelet GP IIb/IIIa blockade in reducing ischemic events before and particularly during PCI in patients with non-ST elevation ACS [9,10,21,22]. This benefit of platelet GP IIb/IIIa inhibition is additive to that conferred by aspirin and unfractionated heparin and is most evident in

those patients undergoing early PCI (<72 h following enrollment) [23]. In summary, adjunctive pharmacotherapy with either low molecular weight heparin or platelet GP IIb/IIIa blockade can improve clinical outcomes of patients with non-ST elevation ACS, particularly when administered in sequence with early coronary revascularization.

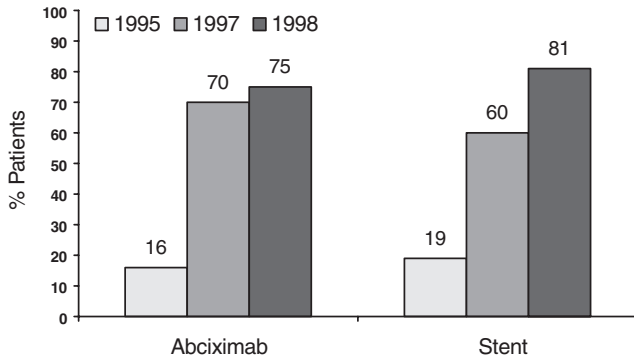
Revascularization strategies

Coronary stents may improve clinical outcomes in patients with unstable angina pectoris when compared with the results obtained with standard balloon angioplasty. In a nonrandomized observational experience, stents (versus balloon angioplasty) improved procedural success and reduced death or the requirement for CABG in hospital [24]. Nevertheless, major adverse cardiovascular events are increased in patients with unstable angina following coronary stent deployment [25,26]. Patients with non-ST segment elevation ACS have abnormalities in platelet size and function [27,28] that may be protracted following presentation [29]. This state of 'platelet hyperactivity' may in part explain the previously observed hazard of early PCI [3–5]. Conversely, adjunctive pharmacotherapy with prophylactic abciximab during PCI (particularly stent deployment) significantly reduces periprocedural complications, improves clinical outcomes and confers a long-term (≥ 1 year) survival advantage in patients with ACS [30–32]. The survival advantage accrued by patients treated with abciximab cannot be ascribed to stent deployment alone [33]. In the absence of adjunctive abciximab therapy, coronary stents have not been associated with a mortality reduction [34].

'Hazard' of early intervention: dispelling the myth

Recent data lead us to question the prior doctrine that early coronary revascularization is fraught with hazard in patients with non-ST elevation ACS. For example, the 1999 United States National Heart, Lung, and Blood Institute (NHLBI) Dynamic Registry demonstrates no increase in major hospital complications following 'ad hoc' PCI [35], despite the more frequent presence of unstable angina and angiographically demonstrable coronary thrombus in these patients. Coronary stents were deployed in almost 70% and adjunctive platelet GP IIb/IIIa blockade was administered in 36% of patients undergoing ad hoc PCI [35]. In a separate report from the NHLBI Dynamic Registry [36], major hospital complications (death, Q-wave myocardial infarction or urgent bypass surgery) were infrequently observed in patients undergoing PCI for non-ST segment elevation myocardial infarction. Adjunctive platelet GP IIb/IIIa blockade was administered in 45% of these PCI procedures. These observations reflect improvements in interventional technology and adjunctive pharmacology. Furthermore, the 1996 New York State Cardiac Surgery database for CABG following non-Q wave myocardial infarction

Figure 1



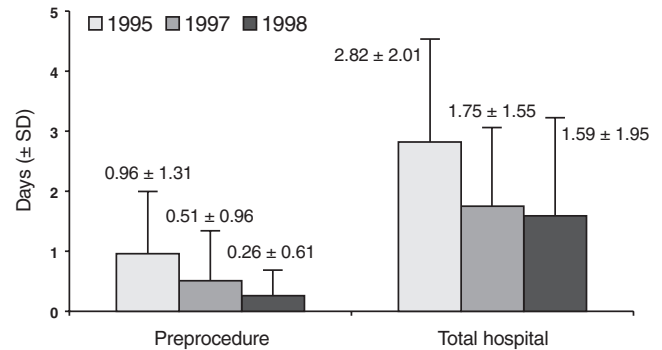
Percentage utilization of abciximab or coronary stents to treat unstable angina by Ohio Heart Health Center Operators at The Christ Hospital, Cincinnati, Ohio, USA for each treatment cohort. Adapted with permission from [39].

demonstrates no increase in risk for mortality (adjusted odds ratio [95% confidence interval] = 1.01 [0.51, 1.98]) when surgery is performed 3–8 days following presentation when compared with CABG for all other classes of angina (mortality 1.3%) [37]. This experience stands in stark contrast to the 12% in-hospital mortality reported from the VANQWISH trial when CABG was performed during the initial hospitalization for non-Q wave myocardial infarction [1].

The Ohio Heart Health Center experience

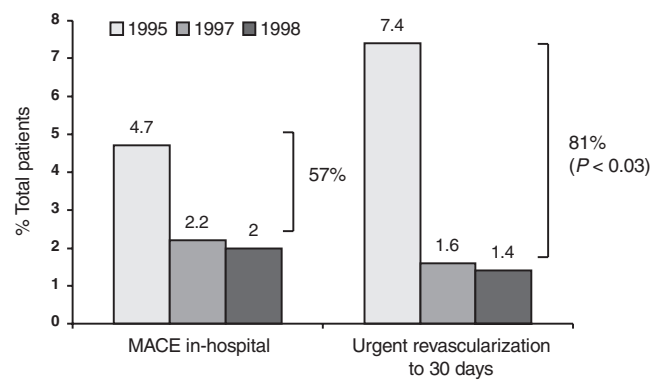
In 1996, abciximab was incorporated into a practice guideline for patients undergoing PCI by Ohio Heart Health Center (OHHC) operators at The Christ Hospital in Cincinnati, Ohio, USA. To assess the impact of this strategy, three separate cohorts of unstable angina patients having PCI either before (1995) or after (1997, 1998) implementation of guideline-driven abciximab therapy were compared [38,39]. No differences in clinical or angiographic demographics were observed between cohorts. The utilization of both abciximab and coronary stents increased in each cohort (Fig. 1). Average preprocedural hospital length of stay was reduced from 0.96 (1995) to 0.26 (1998) days and total hospital stay from 2.82 (1995) to 1.59 (1998) days, respectively (Fig. 2). This abbreviated hospital length of stay was observed in 352 consecutive patients treated in 1998 and compares favorably with the established 4–14 day length of stay for unstable angina pectoris noted previously [13–15]. The same OHHC operators achieved a 57% reduction in major cardiac events (death, Q-wave myocardial infarction or urgent revascularization) in-hospital and an 81% reduction in the requirement for urgent revascularization within 30 days following PCI (Fig. 3). The cost increment of technology (stents and abciximab) was more than offset by cost savings attributable to the reductions in both hospital length of stay and costly adverse

Figure 2



Preprocedural (mean ± SD) and total hospital length of stay for each treatment cohort.

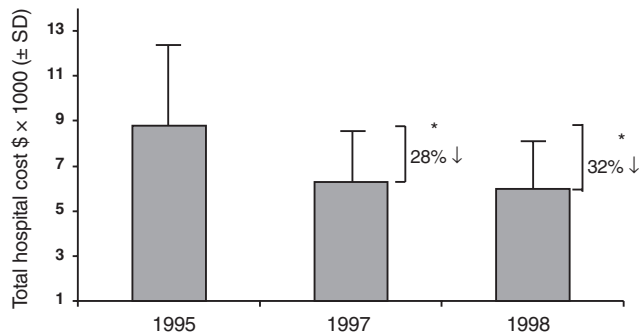
Figure 3



Incidence of occurrence in-hospital of major adverse cardiac events (MACE: death, Q-wave myocardial infarction [QMI], urgent coronary revascularization) following PCI, and the requirement for urgent revascularization (percutaneous or surgical) within 30 days by treatment cohort. Adapted with permission from [39].

clinical outcomes (Fig. 4). Other factors contributing to the reduced cost of care may have included a dedicated, high volume interventional unit, capitated vendor contracts for catheterization laboratory resources and an active clinical research program. Similar improvement in clinical outcomes and a net cost reduction associated with adjunctive abciximab use during PCI in patients with non-ST elevation ACS was reported by Lundstrom *et al* [40]. These investigators observed a reduction in the requirement for urgent revascularization as well as in total costs to 6 months following PCI with adjunctive abciximab. A recently published observational study lends further support for an aggressive, ‘early invasive’ approach to patients who present with non-ST elevation myocardial infarction [41]. Patient and procedural demographics, hospital and long-term outcomes in patients treated for

Figure 4



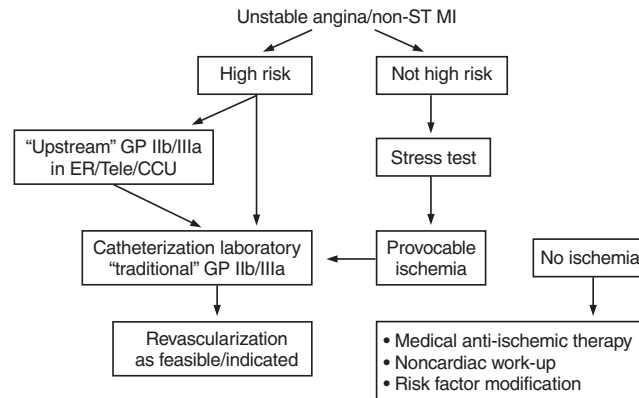
Average total hospital cost (mean ± SD) for treating a patient with unstable angina for each treatment cohort. Total cost includes the cost of abciximab and coronary stents. * $P \leq 0.00005$. Adapted with permission from [39].

non-ST elevation myocardial infarction in hospitals favoring an early invasive treatment strategy were compared with similar data derived from hospitals favoring a noninterventional or 'early conservative' approach. Coronary angiography was performed in 90% of patients and early PCI (≤ 6 h) in almost half of all patients admitted to early invasive hospitals [41]. Acknowledging significant differences in baseline demographics between the patients treated at conservative versus invasive institutions, both in-hospital and late (4 year) survival was improved in aggressively treated patients [41].

Appropriate patient selection

Significant improvements in the ability to risk-stratify patients who present with non-ST elevation ACS have evolved. The single most accurate and readily available predictor in this population is the serum troponin level. Elevation in the serum level of either troponin T or I predicts adverse clinical outcomes [42–44]. A quantitative relationship between troponin level and risk of death, myocardial infarction or urgent revascularization has been established [45]. Troponin is a surrogate marker for platelet-thrombus formation, microvascular embolization and minor myocardial injury. In addition to predicting risk, an elevated troponin level also predicts a beneficial response to abciximab therapy [46]. Similar observations have been made between elevation in serum troponin level and a beneficial response to therapy with intravenous tirofiban or subcutaneous dalteparin in patients with non-ST elevation ACS [47]. Thus, troponin predicts magnitude of clinical benefit from therapy with either platelet GP IIb/IIIa blockade or low molecular weight heparin. Another predictor of risk in patients with non-ST elevation ACS is the 12-lead electrocardiogram [2,48]. Both the presence and magnitude of ST segment depression on the 12-lead electrocardiogram correlate directly with mortality in follow-up

Figure 5



Proposed algorithm for assessment and treatment of patients with unstable angina or non-ST segment elevation myocardial infarction (MI). Patients judged to be at high risk on the basis of symptom complex, electrocardiographic ST segment depression or elevation in serum troponin level are eligible for adjunctive platelet GP IIb/IIIa inhibitor therapy and early coronary angiography. ER, emergency room; Tele, telemetry; CCU, coronary care unit. Adapted with permission from [39].

[2,48]. Patients who manifest signs of left ventricular decompensation or ischemic mitral valve dysfunction during episodes of angina should also be considered high risk. Anginal symptoms (Braunwald classification) define risk for subsequent adverse outcomes. Braunwald Class III angina (rest pain < 48 h) predicts the subsequent occurrence of death or myocardial infarction and Class c (medically refractory angina) adversely affects survival to 30 days [49]. The correlation between Braunwald symptom class and subsequent occurrence of ischemic events may be explained in part by the correlation between symptom class and the presence of thrombus on selective coronary angiography [50,51].

Conclusion: defining appropriate care

Patients with non-ST elevation ACS should be risk-stratified upon presentation. Risk can be assessed by angina symptom class, presence or absence of hemodynamic compromise, electrocardiographic ST segment depression and elevation in serum troponin (Fig. 5). Patients at high risk should undergo early angiography and revascularization as indicated. Patients who have elevated serum troponin should receive therapy with platelet GP IIb/IIIa blockade and/or low molecular weight heparin. If PCI is performed, coronary stent deployment is desirable and adjunctive GP IIb/IIIa blockade is indicated unless a specific contraindication is present. Optimal long-term outcomes, specifically a survival advantage, are conferred by adjunctive abciximab therapy during PCI. Furthermore, CABG performed 3–8 days following presentation for non-ST elevation infarction is not associated with

increased risk for mortality. Patients determined to be not at high risk should undergo appropriate diagnostic testing. Thus, efficient and effective therapy can now be offered to patients with non-ST elevation ACS. Empirically defined periods of medical stabilization most likely add cost without incremental benefit.

References

1. Boden WE, O'Rourke RA, Crawford MH, Blaustein AS, Deedwania PC, Zoble RG, Wexler LF, Kleiger RE, Pepine CJ, Ferry DR, Chow BK, Lavori PW: **Outcomes in patients with acute non-Q wave myocardial infarction randomly assigned to an invasive, as compared with a conservative, management strategy.** *N Engl J Med* 1998, **338**:1785-1792.
2. Anderson HV, Cannon CP, Stone PH, Williams DO, McCabe CH, Knatterud EL, Thompson B, Willerson JT, Braunwald E, for the TIMI IIIB investigators: **One year results of the Thrombolysis in Myocardial Infarction (TIMI) IIIB clinical trial; a randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave myocardial infarction.** *J Am Coll Cardiol* 1995, **26**:1643-1650.
3. Hartzler GO, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV: **"High risk" percutaneous transluminal coronary angioplasty.** *Am J Cardiol* 1988, **61**:33G-37G.
4. Adele C, Vaitkus PT, Wells SW, Zehnacker JB: **Cost advantages of an ad hoc angioplasty strategy.** *J Am Coll Cardiol* 1998, **31**:321-325.
5. Myler RK, Shaw RE, Stertzer SH, Bashour TT, Ryan C, Hecht HS: **Unstable angina and coronary angioplasty.** *Circulation* 1990, **82** (suppl):88-95.
6. Braunwald E, Mark DB, Jones RH, Cheitlin MD, Fuster V, McCauley KM, Edwards C, Green LA, Mushlin AI, Swain JA, Smith EE, Cowan M, Rose GC, Concannon CA, Grines CL, Brown L, Lytle BW, Goldman L, Topol EJ, Willerson JT, Brown J, Archibald N: *Unstable Angina: Diagnosis and Management.* Rockville, MD: Agency for health care policy and research and the National Heart, Lung and Blood Institute, Public Health Service. U.S. Department of Health and Human Services; 1994; AHCPR Publication No. 94-0602.
7. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIa Investigators: **Randomized trial of intravenous heparin versus recombinant hirudin for acute coronary syndromes.** *Circulation* 1994, **90**:1631-1637.
8. Cohen M, Demers C, Garfinkel EP, Turpie AG, Fromell GJ, Goodman S, Langer A, Califf RM, Fox KA, Premmereur J, Bigonzi F: **A comparison of low-molecular weight heparin with unfractionated heparin for unstable coronary artery disease.** *N Engl J Med* 1997, **337**:447-452.
9. The Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study Investigators: **Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction.** *N Engl J Med* 1998, **338**:1488-1497.
10. The PURSUIT Trial investigators: **Inhibition of platelet glycoprotein IIb/IIIa with eptifibatid in patients with acute coronary syndromes.** *N Engl J Med* 1998, **339**:436-443.
11. The PARAGON Investigators: **International, randomized, controlled trial of lamifiban (a platelet glycoprotein IIb/IIIa inhibitor), heparin, or both in unstable angina.** *Circulation* 1998, **97**:2386-2395.
12. van Domburg RT, Miltenburg-vanZijl AJ, Veerhoek RJ, Simoons ML: **Unstable angina: good long-term outcome after a complicated early course.** *J Am Coll Cardiol* 1998, **31**:1534-1539.
13. Yusuf S, Flather M, Pogue J, Hunt D, Varigos J, Piegas L, Avezum A, Anderson J, Keltai M, Budaj A, Fox K, Ceremuzynski L, for the Organization to Assess Strategies for Ischemic Syndromes (OASIS) registry investigators: **Variations between countries in invasive cardiac procedures and outcomes in patients with suspected unstable angina or myocardial infarction without initial ST elevation.** *Lancet* 1998, **352**:507-514.
14. Scirica BM, Moliterno DJ, Every NR, Anderson HV, Aguirre FV, Granger CB, Lambrew CT, Rabbani LE, Sapp SK, Booth JE, Ferguson JJ, Cannon CP, and the GUARANTEE Investigators: **Racial differences in the management of unstable angina: results from the multicenter GUARANTEE registry.** *Am Heart J* 1999, **138**:1065-1072.
15. Fox KA, Kokkinos DV, Deckers J, Keil U, Maggioni A, Steg G on behalf of the ENACT (European Network for Acute Coronary Treatment) Investigators: **The ENACT study: a pan-European survey of acute coronary syndromes.** *Eur Heart J* 2000, in press.
16. Lindahl B, Venge P, Wallentin L on behalf of Fragmin in Unstable Coronary Artery Disease (FRISC) study group: **Troponin T identifies patients with unstable coronary artery disease who benefit from long-term antithrombotic protection.** *J Am Coll Cardiol* 1997, **29**:43-48.
17. Antman EM, McCabe CH, Gurfinkel EP, Turpie AG, Bernink PJ, Salein D, Bayes De Luna A, Fox K, Lablanche JM, Radley D, Premmereur J, Bruamwald E: **Enoxaparin prevents death and cardiac Ischemic events in unstable angina/non-Q-wave myocardial infarction: results of the Thrombolysis in Myocardial Infarction (TIMI) IIb trial.** *Circulation* 1999, **100**:1593-1601.
18. Fragmin and Fast Revascularisation during InStability in Coronary artery disease (FRISC II) Investigators: **Long-term low molecular mass heparin in unstable coronary-artery disease.** *Lancet* 1999, **354**:701-707.
19. Fragmin and Fast Revascularisation during InStability in Coronary artery disease (FRISC II) Investigators: **Invasive compared with non-invasive treatment in unstable coronary-artery disease.** *Lancet* 1999, **354**:708-715.
20. Collett JP, Montalescot G, Probinski G, Tanagano F, Lison L, Annick A, Sotirov I, Choussat R, Thomas D: **PTCA without heparin and without coagulation monitoring in unstable angina patients pre-treated with subcutaneous enoxaparin [abstract].** *Circulation* 1999, **100**:I-188.
21. CAPTURE Investigators: **Randomized placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina: the CAPTURE Study.** *Lancet* 1997, **349**:1429-1435.
22. Boersma E, Akkerhuis M, Theroux P, Califf RM, Topol EJ, Simoons ML: **Platelet glycoprotein IIb/IIIa receptor inhibition in non-ST-elevation acute coronary syndromes. Early benefit during medical treatment only, with additional protection during percutaneous coronary intervention.** *Circulation* 1999, **100**:2045-2048.
23. Kleiman NS, Lincoff AM, Flaker GC, Pieper KS, Wilcox RG, Berdan LG, Lorenz TJ, Cokkinos DV, Simoons ML, Boersma E, Topol EJ, Califf RM, Harrington RA for the PURSUIT investigators: **Early percutaneous coronary intervention, platelet inhibition with eptifibatid, and clinical outcomes in patients with acute coronary syndromes.** *Circulation* 2000, **201**:751-757.
24. Singh M, Holmes DR, Garratt KN, Bell MR, Berger PB, Rihal CS, Schwartz RS, Hammes L: **Stents versus conventional PTCA in unstable angina [abstract].** *J Am Coll Cardiol* 1999, **33**:29A.
25. Angioi M, Danchin N, Gangloff C, Grentzinger A, Jacquemin L, Berder V, Houplon P, Julliere Y, Cherrier F: **Ticlopidine-aspirin as antithrombotic regimen for intracoronary stenting for unstable angina: is there a need for further antiplatelet therapy? [abstract].** *J Am Coll Cardiol* 1998, **31**:100A.
26. Kastrati A, Neumann FJ, Schomig A: **Operator volume and outcome of patients undergoing coronary stent placement.** *J Am Coll Cardiol* 1998, **32**:970-978.
27. Lu Y, Theroux P, Xiao Z, Ghitescu M: **Increased expression of GP IIb/IIIa platelet membrane receptor in acute ischemic syndromes [abstract].** *Circulation* 1996, **94**(suppl I):I-515.
28. Pizulli L, Yang A, Martin JF, Luderitz B: **Changes in platelet size and count in unstable angina compared to stable angina or non-cardiac chest pain.** *Eur Heart J* 1998, **19**:80-84.
29. Ault KA, Cannon CP, Mitchell J, McCahan J, Tracy RP, Novotny WF, Reimann JD, Braunwald E: **Platelet activation in patients after an acute coronary syndrome: results from the TIMI-12 trial.** *J Am Coll Cardiol* 1999, **33**:634-639.
30. Lincoff AM, Califf RM, Anderson KM, Weisman HF, Aguirre FV, Kleiman NS, Harrington RA, Topol EJ, for the EPIC Investigators: **Evidence for prevention of death and myocardial infarction with platelet membrane glycoprotein IIb/IIIa receptor blockade by abciximab (7E3 Fab) among patients with unstable angina undergoing percutaneous coronary revascularization.** *J Am Coll Cardiol* 1997, **30**:149-156.
31. Topol EJ, Mark DB, Lincoff AM, Cohen E, Burton J, Kleiman N, Talley D, Sapp S, Booth J, Cabot CF, Anderson K, Califf RM, on behalf of the EPISTENT Investigators: **Outcomes of 1 year and economic implications of platelet IIb/IIIa blockade in patients undergoing coronary stenting: results from a multicentre randomised trial.** *Lancet* 1999, **354**:2019-2024.

32. Topol EJ, Ferguson JJ, Weisman HF, Tcheng JE, Ellis SG, Kleiman NS, Ivanhoe RJ, Wang AL, Miller DP, Anderson KM, Califf RM, for the EPIC Investigator Group: **Long-term protection from myocardial ischemic events in a randomized trial of brief integrin β 3 blockade with percutaneous coronary intervention.** *JAMA* 1997, **278**:479–484.
33. Bhatt DL, Lincoff AM, Califf RM, Simoons ML, Tcheng JE, Brener SJ, Wolski KE and Topol EJ: **The benefit of abciximab in interventional cardiology is not device-specific.** *Am J Cardiol* 2000, **85**:1060–1064.
34. Kong DF, Hasselblad V, Tcheng JE, Ohman EM, Topol EJ, Califf RM: **Clinical outcome improvements from coronary stenting: a systematic overview [abstract].** *Eur Heart J* 1998, **19**:571.
35. Jacobs AK, Laskey WK, Vlachos H, Cowley MJ, Faxon DP, Williams DO, Detre KM: **Outcome of patients undergoing coronary intervention at the time of diagnostic catheterization: A report from the 1999 Dynamic Registry [abstract].** *J Am Coll Cardiol* 2000, **35**:12A.
36. Williams DO, Yeh W, Detre KM, Kelsey SF, Cohen H, Cowley MJ, Al-Bassam M, Jacobs AK, Bourassa M: **Percutaneous coronary intervention for non-ST elevation myocardial infarction: a report from the NHLBI Dynamic Registry [abstract].** *J Am Coll Cardiol* 2000, **35**:39A.
37. Menon V, Homel P, Kamel SM, Fincke R, Swistel DG, Hochman JS: **Mortality with coronary artery bypass grafting for non Q MI; results from the 1996 New York State Cardiac Surgery database [abstract].** *J Am Coll Cardiol* 2000, **35**:347A.
38. Kereiakes DJ: **Preferential benefit of platelet glycoprotein IIb/IIIa receptor blockade: specific considerations by device and disease state.** *Am J Cardiol* 1998, **81**:49E–54E.
39. Kereiakes DJ, McDonald M, Broderick TB, Roth EM, Whang DD, Martin LH, Howard WL, Schneider J, Shimshak T, Abbottsmith CW: **Platelet glycoprotein IIb/IIIa receptor blockers: an appropriate use model for expediting care in acute coronary syndromes.** *Am Heart J* 2000, **139** (suppl):S53–S60.
40. Lundstrom RJ, Colby CJ, Jindeel A, Hay RL: **Abciximab in unstable coronary syndromes: benefits and costs in a group model non-profit health maintenance organization [abstract].** *J Am Coll Cardiol* 1999, **33**:41A.
41. Scull GS, Martin JS, Weaver D, Every NR, for the MITI Investigators: **Early angiography versus conservative treatment in patients with non-ST elevation acute myocardial infarction.** *J Am Coll Cardiol* 2000, **35**:895–902.
42. Ohman EM, Armstrong PW, Christenson RH, Granger CB, Katus HA, Hamm CW, O'Hanesian MA, Wagner GS, Kleiman NS, Harrell FE Jr, Califf RM, Topol EJ for the GUSTO IIa Investigators: **Cardiac troponin T levels for risk stratification in acute myocardial ischemia.** *N Engl J Med* 1996, **335**:1333–1341.
43. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E: **Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes.** *N Engl J Med* 1996, **335**:1342–1349.
44. Roberts R, Fromm RE: **Management of acute coronary syndromes based on risk stratification by biochemical markers: an idea whose time has come.** *Circulation* 1998, **98**:1831–1833.
45. Lindahl B, Venge P, Wallentin L on behalf of the FRISC study group: **Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease.** *Circulation* 1996, **93**: 1651–1657.
46. Hamm CW, Heeschen C, Goldmann B, Vahanian A, Adgey J, Miguel CM, Rutsch W et al for the C7E3 Fab Antiplatelet Therapy in Unstable Refractory Angina (CAPTURE) study investigators: **Benefit of abciximab in patients with refractory unstable angina in relation to serum troponin T levels.** *N Engl J Med* 1999, **340**:1623–1629.
47. Heeschen C, Hamm CS, Goldmann B, Deu A, Langenbrink L, White HD: **Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban.** PRISM Study Investigators: **Platelet Receptor Inhibition in Ischemic Syndrome Management.** *Lancet* 1999, **354**:1757–1762.
48. Hyde TA, French JK, Wong CK, Strazinicky IT, Whitlock RM, White HD: **Four-year survival of patients with acute coronary syndromes without ST-segment elevation and prognostic significance of 0.5-mm ST-segment depression.** *Am J Cardiol* 1999, **84**:379–385.
49. Bazzino O, Diaz R, Tajer C, Paviottic, Mele E, Trivi M, Piombo A, Prado AH, Paolasso E for the ECLA collaborative group: **Clinical predictors of in-hospital prognosis in unstable angina: ECLA 3.** *Am Heart J* 1999, **137**:322–331.
50. Owa M, Origasa H, Saito M: **Predictive validity of the Braunwald classification of unstable angina for angiographic findings, short-term prognoses, and treatment selection.** *Angiology* 1997, **48**:663–671.
51. Dangas G, Mehran R, Wallenstein S, Courcoutsakis NA, Kakarala V, Hollywood J, Ambrose JA: **Correlation of angiographic morphology and clinical presentation in unstable angina.** *J Am Coll Cardiol* 1997, **29**:519–525.

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